

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (original) A method of assessing a disease condition in an individual comprising;
contacting said nucleosomes from a biological fluid sample obtained from the individual with an antibody which binds specifically with a modified histone protein,
wherein binding of said antibody to said nucleosomes is indicative that the individual has a disease condition.
2. (original) A method according to claim 1 wherein said nucleosomes are concentrated from the biological fluid sample.
3. (currently amended) A method according to claim 1 ~~or claim 2~~ wherein the disease condition is a cancer condition or an autoimmune disease.
4. (currently amended) A method according to ~~any one of the preceding claims~~ claim 1 wherein the modified histone has a modification shown in Table 1.
5. (currently amended) A method according to ~~any one of the preceding claims~~ claim 1 wherein the modified histone has a modification shown in Table 2.

6. (currently amended) A method according to ~~any one of the preceding claims~~ claim 1 wherein said antibody comprises a detectable label.

7. (original) A method of assessing histone modification in nucleosomes in a biological fluid sample from an individual comprising;

contacting a biological fluid sample from said individual with a first antibody,
determining binding of said first antibody to a nucleosome containing a histone modification using a second antibody,

wherein one of said first or second antibodies binds to a nucleosome and the other of said first or second antibodies binds specifically to a modified histone.

8. (original) A method according to claim 7 wherein said first antibody binds to nucleosomes and the second antibody binds specifically to the modified histone.

9. (original) A method according to claim 7 wherein the second antibody binds to nucleosomes and the first antibody binds specifically to the modified histone.

10. (currently amended) A method according to ~~any one of claims 7 to 9~~ claim 7 wherein the modified histone comprises a modification shown in Table 1.

11. (currently amended) A method according to ~~any one of claims 7 to 9~~ claim 7 wherein the modified histone comprises a modification shown in Table 2.

12. (currently amended) A method wherein according to ~~any one of claims 7 to 11~~ claim 7 the biological fluid sample is a plasma or serum sample.

13. (currently amended) A method according to ~~any one of claims 7 to 12~~ claim 7 wherein said first or said second antibody is immobilised.

14. (original) A method according to claim 13 wherein the non-immobilised antibody of said first and second antibodies comprises a detectable label.

15. (original) A method of assessing histone modification in cell-free nucleosomes in a biological fluid sample comprising;

contacting a biological fluid sample with an antibody which binds specifically to a histone comprising a modification,

determining the binding of said antibody to nucleosomes in said sample,

the binding of said antibody being indicative of the presence of modified histone in nucleosomes in the blood of said individual.

16. (original) A method according to claim 15 wherein the modification is a modification shown in Table 1.

17. (currently amended) A method according to claim 15 ~~or claim 16~~ wherein the modification is a modification shown in Table 2.

18. (currently amended) A method according to ~~any one of claims 15 to 17~~ claim 15 wherein the disease condition is a cancer condition or an autoimmune disease.

19. (currently amended) A method according to ~~any one of claims 15 to 18~~ claim 15 wherein said antibody comprises a detectable label.

20. (original) A method of diagnosing a cancer condition in an individual comprising;
 contacting biological fluid sample obtained from an individual with an antibody
which binds specifically to a modified histone,
 determining the binding of said antibody to nucleosomes in said sample,
 the binding of said antibody to nucleosomes in said sample being indicative that
said individual has a cancer condition.

21. (original) A method according to claim 20 wherein the disease condition is a cancer condition or an autoimmune disease.

22. (currently amended) A method according to claim 20 ~~or claim 21~~ wherein the modified histone has a modification shown in Table 1.

23. (currently amended) A method according to ~~any one of claims 20 to 22~~ claim 20
wherein the modified histone has a modification shown in Table 2

24. (currently amended) A method according to ~~any one of claims 20 to 23~~ claim 20
wherein said modification is not H2B Ser 14 (P).

25. (currently amended) A method according to ~~any one of claims 20 to 24~~ claim 20
wherein said antibody comprises a detectable label.

26. (currently amended) A method according to ~~any one of claims 1 to 25~~ claim 1
comprising isolating DNA associated with the nucleosome comprising a modified
histone.

27. (original) A method according to claim 26 comprising amplifying said nucleosome
associated DNA.

28. (currently amended) A method according to claim 26 ~~or claim 27~~ comprising
sequencing said nucleosome associated DNA.

29. (currently amended) A method according to ~~any one of claims 26 to 28~~ claim 26
comprising labelling said nucleosome associated DNA with a detectable label.

30. (currently amended) A method according to ~~any one of claims 26 to 29~~ claim 26 comprising contacting said nucleosome associated DNA with a DNA molecule having a known sequence under conditions suitable for hybridisation and determining hybridisation.

31. (original) A method according to claim 30 wherein said DNA molecule of known sequence is comprised in a microarray.

32. (currently amended) A method according to ~~any one of claims 26 to 31~~ claim 26 claim comprising determining the hybridisation of DNA from said individual which is associated with said histone modification relative to DNA associated with said histone modification from one or more other individuals.

33. (currently amended) A method according to ~~any one of claims 26 to 31~~ claim 26 wherein said modified histone comprises a modification associated with gene silencing.

34. (original) A method according to claim 33 wherein said modification is selected from H3 Lys 9 (Me), H3 Lys 27 (Me), H3 Lys 36 (Me), H3 Lys 79 (Me) and H4 Lys 20 (Me).

35. (currently amended) A method according to ~~any one of claims 26 to 34~~ claim 26 wherein said modified histone comprises a modification associated with gene activation.

36. (original) A method according to claim 35 wherein said modification is selected from H3 Lys 4 (Me), H3 Lys 9 (Ac), H3 Lys 14 (Ac) and H3 Lys 23 (Ac).

37. (original) A method of identifying a tumour suppressor gene comprising;
 contacting biological fluid sample obtained from an individual suffering from a cancer condition with an antibody which binds specifically to a histone having a modification associated with silencing,
 isolating nucleosomes bound to said antibody,
 sequencing DNA associated with said bound nucleosomes, and;
 identifying said DNA as a tumor suppressor gene.

38. (original) A method according to claim 37 wherein said modification is selected from H3 Lys 9 (Me) H3 Lys 27 (Me), H3 Lys 36 (Me), H3 Lys 79 (Me) and H4 Lys 20 (Me).

39. (original) A method of identifying an oncogene comprising;
 contacting biological fluid sample obtained from an individual suffering from a cancer condition with an antibody which binds specifically to a histone having a modification associated with activation,
 isolating nucleosomes bound to said antibody,
 sequencing DNA associated with said bound nucleosomes, and; identifying said DNA as an oncogene.

40. (original) A method according to claim 39 wherein said modified histone comprises a modification shown in Table 1 and/or Table 2.

41. (original) A method of identifying a patient as a responsive to histone modification modulation therapy comprising;

determining the level of histone modification in cell-free nucleosomes within a sample obtained from the patient, relative to a sample obtained from a healthy individual,

a change in the level of modification being indicative that the patient is responsive to histone modification modulation therapy.

42. (original) A method of assessing a patient for a therapeutic treatment comprising;

determining the presence of one or more genes which confer resistance to said treatment in cell-free nucleosomes in a sample obtained from the patient,

wherein said nucleosomes comprise a histone modification associated with activation.

43. (original) A method according to claim 42 wherein said modification is a modification shown in Table 1 and/or Table 2.

44. (original) A method of determining the presence of a cell-free nucleosome having a histone modification comprising;

determining the presence of an antibody which binds specifically to the histone modification in a sample obtained from an individual,

the presence of said antibody being indicative of the presence of said nucleosomes in said individual.

45. (original) A method according to claim 44 comprising contacting the sample with an antigen comprising a histone modification epitope and determining binding to the antigen.

46. (original) A method according to claim 45 wherein said antigen is immobilised on a solid support.

47. (original) A method according to claim 45 wherein said antigen comprises a detectable label.

48. (currently amended) A method according to ~~any one of claims 44 to 47~~ claim 44 wherein said modified histone comprises a modification shown in Table 1 and/or Table 2.